

acid molecule encodes a mammalian methionine synthase reductase polypeptide having at least 20% of the methionine synthase reductase activity of the methionine synthase reductase polypeptide of SEQ ID NO: 2.

60. (Previously Presented) The nucleic acid molecule of claim 59, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide having at least 55% of the methionine synthase reductase activity of the methionine synthase reductase polypeptide of SEQ ID NO: 2.

61. (Previously Presented) The nucleic acid molecule of claim 56, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide that comprises a consensus binding site for one or more cofactors selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises any one of SEQ ID NOs: 25 or 52-61.

62. (Previously Presented) The nucleic acid molecule of claim 56, wherein the polynucleotide sequence of said nucleic acid molecule comprises a mutation or polymorphism present in a naturally-occurring mammalian methionine synthase reductase gene.

63. (Previously Presented) A substantially pure nucleic acid molecule having at least 95% sequence identity to SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47 and encoding a mammalian methionine synthase reductase polypeptide that has a reduced ability to catalyze the reductive methylation of methionine synthase-cob(II)alamin to generate

methionine synthase-cob(III)alamin-CH<sub>3</sub> relative to the methionine synthase reductase activity of a mammalian methionine synthase reductase polypeptide encoded by SEQ ID NO: 1.

64. (Previously Presented) The nucleic acid of claim 63, wherein said nucleic acid molecule has the sequence of SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

65. (Previously Presented) The nucleic acid molecule of claim 63, wherein said nucleic acid molecule encodes a human methionine synthase reductase polypeptide.

66. (Previously Presented) The nucleic acid molecule of claim 63, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide that comprises a consensus binding site for one or more cofactors selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises any one of SEQ ID NOs: 25 or 52-61.

67. (Previously Presented) The nucleic acid molecule of claim 63, wherein the polynucleotide sequence of said nucleic acid molecule comprises a mutation or polymorphism present in a naturally-occurring mammalian methionine synthase reductase gene.

68. (Currently Amended) A substantially pure antisense nucleic acid molecule consisting of ~~having~~ a polynucleotide sequence that is completely complementary to at least 18 contiguous nucleotides of a mammalian methionine synthase reductase gene consisting of ~~having~~

the polynucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

69. (Currently Amended) The antisense nucleic acid molecule of claim 68, wherein said antisense nucleic acid molecule comprises a polynucleotide sequence the complete complement of which encodes a polypeptide consisting of the sequence set forth in ~~comprises a consensus binding site for one or more cofactors present in a selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises~~ any one of SEQ ID NOs: 25 or 52-61.

70. (Previously Presented) The antisense nucleic acid molecule of claim 68, wherein said antisense nucleic acid molecule comprises a polynucleotide sequence the complete complement of which comprises a mutation or polymorphism present in a naturally-occurring mammalian methionine synthase reductase gene.